ORIGINAL ARTICLE

Comparative Study of Dexmedetomidine and Fentanyl as an Adjuvant to Epidural Bupivacaine for Post-operative Pain Relief in Hepato-biliary Pancreatic Surgery

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ABSTRACT

Background: Postoperative pain responsible for neurohumoral changes which may cause various organ dysfunctions, prolong hospitalization and convalescence. Epidural analgesia confers excellent pain relief and complete dynamic analgesia leading to a substantial reduction in the surgical stress response.

Objectives: The aim of the study was to compare the postoperative analgesic effect of dexmedetomidine and fentanyl as an adjuvant to epidural bupivacaine in adult patients undergoing hepatobiliary pancreatic surgery.

Material and method: Eighty(80) patients were selected in the pre anaesthetic checkup room who were going to be operated for hepatobiliary pancreatic disorders. Each patient in group D(Dexmedetomidine group): Dexmedetomidine 2ml (100 μgm) was mixed with 48ml bupivacaine 0.125% in a syringe 50ml and infused epidurally @ 4ml/hr. for the postoperative 48 hours. Group F (fentanyl group): Fentanyl 2ml (100 μgm) was mixed with 48 ml bupivacaine 0.125% in a syringe 50 ml and infused epidurally @ 4ml/hr. for the postoperative 48 hours.

Results: The quality of analgesia was almost similar with dexmedetomidine and fentanyl group but perioperative haemodynamic stability was more in dexmedetomidine group than fentanyl group ($p = < 0.05$). The incidence of post-operative nausea and vomiting, pruritus, urinary retention and respiratory depression significantly lower with dexmedetomidine compared to fentanyl group ($p = < 0.05$).

Conclusion: Dexmedetomidine is an ideal adjuvant to epidural bupivacaine for postoperative analgesia compared to fentanyl in patients undergoing hepatobiliary pancreatic surgery.

Key Words: Dexmedetomidine, fentanyl, epidural bupivacaine, hepatobiliary pancreatic surgery.

Introduction

Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage.[1] Postoperative pain, is typically associated with neuro-endocrine stress response that is proportional to pain intensity. Many patients, however, continues to experience inadequate pain relief.[2] Despite improvements in analgesic delivery, several recent surveys have found that up to 80% of patients report moderate to severe pain after surgery.[3,4,5]

The postoperative pain scores are lowered by using multimodal analgesia and continuous epidural analgesia.[6] Opioid and local anaesthetic infusion by an epidural catheter is widely used as a postoperative pain management method after major abdominal surgeries.[7] There are several methods now a days to provide sufficient analgesia. The

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agents which cause less side effects but better quality of analgesia is more valuable.

Epidural opioids with or without local anaesthetics provides a postoperative pain relief, but it is associated with many side effects. Opioids like fentanyl have been used traditionally as an adjunct for epidural administration in combination with a lower dose of local anaesthetic to achieve the desired anaesthetic effect.[8] Fentanyl acts as an agonist at μ-opioid receptors to enhance the analgesia, it is 100 times more potent than morphine.

Dexmedetomidine is a highly selective α_2 adrenergic receptor agonist, and it has a sedative, anxiolytic, analgesic, antihypertensive and sympatholytic properties.[9] It improves the quality of perioperative anaesthesia and analgesia.[10] Dexmedetomidine does cause a manageable hypotension and bradycardia but the striking feature of this drug is the lack of opioid-relate side effects like respiratory depression, pruritis, nausea, and vomiting.[11,12]

Our goal in this prospective, single blind, randomized study was to compare the postoperative analgesic effect of dexmedetomidine and fentanyl as an adjuvant to continuous epidural bupivacaine with their side effects in adult patients undergoing hepatobiliary pancreatic surgeries.

Materials & Methods

This randomized single-blind study was conducted from 1st January, 2015 to 31st December, 2016 at the department of Anaesthesiology and Surgical ICU, BIRDEM General Hospital, Shahbagh, Dhaka, Bangladesh. After institutional ethical committee approval and informed written consent, a total number of 80 adult patients with ASA physical status I&II scheduled for various elective hepatobiliary and pancreatic surgeries under combined anaesthesia (General plus Epidural) were enrolled in this study. All patients were reassured and the anaesthetic procedure was explained on the day before the operation. Intravenous access established in all patients in the operating room with base line arterial blood pressure (non-invasively) and heart rate obtained. Every patient was received an epidural block in the sitting position at the T8-9 or T9-10 level via 18 G Touhy needle. After epidural insertion each patient received 6 - 8 ml 0.125% inj. Bupivacaine through epidural catheter. Each patient received General anaesthesia with induction dose of inj. Fentanyl 2 microgram/kg, inj. Propofol 2mg/kg and muscle relaxant inj. Atracurium 0.5mg/kg. After induction, general anaesthesia was maintained by 60% N_2O and 40% O_2 and continuous infusion of Propofol @ 4mg/kg/hr. - 6mg/kg/hr. An incremental dose of muscle relaxant inj. Atracurium 1/4th of initial dose was given every 20 minutes interval. The base line blood pressure and heart rate were recorded from the same noninvasive monitor and cardiac rate and rhythm were also monitored from a continuous display of E.C.G from lead II.

After extubation patients were transferred to recovery room. Analgesia was given in the immediate postoperative period (0 hr.) and they were divided into two groups 40 in each group randomly allocated by envelop method where Each patient in group D(Dexmedetomidine group): Dexmedetomidine 2ml(100 μg) was mixed with 48ml bupivacaine 0.125% in a syringe 50 ml and infused epidurally @ 4ml/hr. for the postoperative 48 hours. Group F (fentanyl group): Fentanyl 2 ml (100 μg) was mixed with 48 ml bupivacaine 0.125% in a syringe 50 ml and infused epidurally @ 4ml/hr. for the postoperative 48 hours.

Visual analogue score (VAS), noninvasive blood pressure, heart rate, oxygen saturation, respiratory rate was recorded in every patient. All parameters were recorded at 0 hour, 1 hour, 3 hour, 6 hour, 9 hour, 12 hour, 18 hour, 24 hour, 30 hour, 36 hour and 48 hour after surgery.

Each patient in group D received 0.125% bupivacaine with 2 μgm. dexmedetomidine / ml solution through epidural catheter @ 4 ml / hr. and group F received 0.125% bupivacaine with 2 μgm. fentanyl / ml solution through epidural catheter@ 4 ml / hr. just 15 minute after general anaesthesia.

Post-operative pain was assessed by visual analogue scale (VAS) which is a simple and often used method for evaluating variations in pain intensity. Subjects were instructed to indicate the intensity of the pain by marking a 10 cm line anchored with

terms describing the extremes of pain intensity. VAS pain scale was 10 cm vertical lines anchored with "no pain" at the bottom and "worst imaginable pain" at the top. Visual analogue score (VAS) was recorded at 0 hour, 1 hour, 3 hour, 6 hour, 9 hour, 12 hour, 18 hour, 24 hour, 30 hour, 36 hour and 48 hour after surgery (VAS; 0 - 10 cm; 0 = no pain and 10 = worst possible pain).

Data Processing

All data presented as mean (standard deviation) unless otherwise indicated. Analysis of variance unpaired student t test and chi-square test used to detect the demographic data among the two groups. Chi-square test, with any correction needed (e.g., Yates's continuity correction) used to analyze the collected data. Data collected on a predesigned data collection sheet and later on compiled on a master chart. A p value of <0.05 accepted as statistically significant. Statistical analysis carried out using Statistical Package for Social Science (SPSS) for Windows version 17.0.

Results

Eighty patients who underwent Hepatobilliary and pancreatic surgery were enrolled in the study. Among them 51 male and 29 female. Demographic data for each group was similar (Table 1). Sixteen patients (20%) underwent Whipple's procedure, thirty six patients (45%) underwent triple bypass & twenty eight (35%) patients underwent biliary reconstruction (Table 2). Mean duration of surgery for Whipple's procedure 4 hours, for Triple bypass 3.5 hours and for biliary reconstruction 3.12 hours (Table 2). The peroperative heart rate (Figure 1) and mean arterial blood pressure (Figure 2) decreased in both groups but the decrease was more in patients of dexmedetomidine group than fentanyl group and the comparison was significant between the groups ($p<0.05$).

In the postoperative period the heart rate (Table 3) and the mean arterial blood pressure (Table 4) were decreased in both groups but more decreased in group D that was dexmedetomidine group which was statistically significant ($p<0.05$).

Postoperative satisfaction with the epidural analgesia was similar with median scores of 69 (levobupivacaine) and 73(bupivacaine) (VAS; 100mm= extremely satisfied) in the first 48 hour after operation (Figure 3). No statistical significant were observed in between groups ($p>0.05$)

Total drug consumption for group D was 220 ml and for group F was 260 ml. Additional drug was needed for group D 44 ml and for group F 56ml .

Table 5 showed that the postoperative complications like nausea and vomiting, pruritus, urinary retention and respiratory depression were significantly lower in dexmedetomidine group compared to fentanyl group ($p<0.05$) and there was no significant difference in the incidence of headache or shivering between the two groups ($p>0.05$).

Sixty patients Epidural catheter were inserted at the level of T8/9 out of which fourty two patients were group D and eighteen patients were group F. In twenty patient Epidural catheter were inserted at the level of T9/10 out of which eight patients were in group D and twelve patients were in group F.

ASA catagorization (I, II) of group D was 30/12 and of group B was 22/16 patients. No cases of cardiac depression or central nervous system toxicity caused by vascular absorption or direct intravascular injection of local anaesthetic occurred. Our postoperative repeated visits for early detection of pain and provide increased patient satisfaction.

Table 1: Demographic variables

Variables	Group-D	Group-F	p value
Age (years)	50.40±11.12	52.20±12.55	0.56^{ns}
Sex (M/F)	26/14	25/15	0.78^{ns}
Weight (kg)	65.30±9.44	66.67±8.13	0.55^{ns}

All values were presented as mean±SD or in frequencies. Data were analysed using unpaired student t-test. Statistically significance was set at p-value <0.05. (S=significance, NS=not significant)

Table 2: Distribution of the patients by type and duration of operation (n=80)

Types of operation	Frequency	Percentage (%)	Duration of operation (hours) Mean±SD
		20.0	
Whilples	16	45.0	4.0±1.12
Triple bypass	36	35.0	3.5±0.85
Biliary reconstruction	28	100.0	3.12±0.75
Total	80		3.54±0.60

All values were presented as mean±SD or in frequencies. Data were analysed using unpaired student t-test. Statistically significance was set at p-value <0.05. (S=significance, NS=not significant)

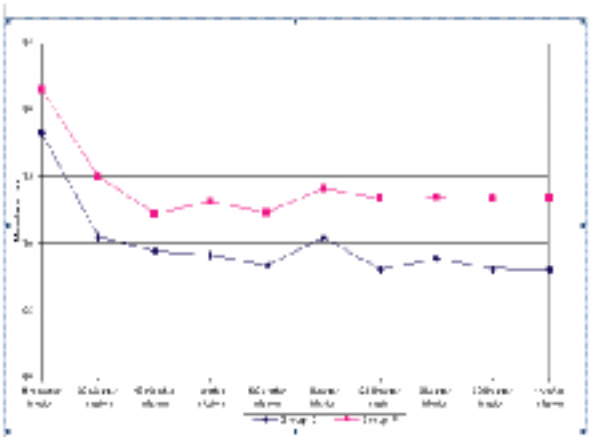
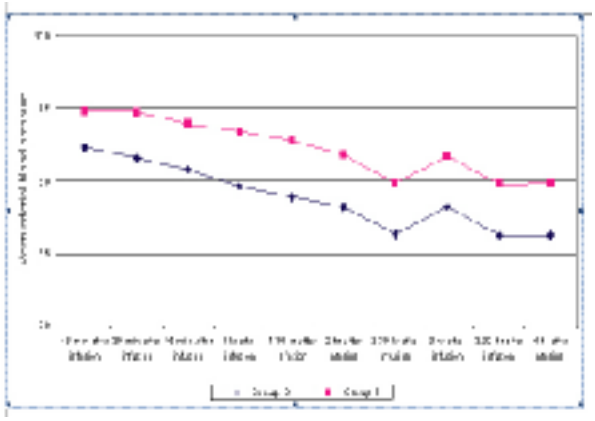


Figure- 2: Line diagram showing peroperative mean arterial blood pressure in two groups



The mean arterial blood pressure at different time in peroperative period compared between two groups. Statistical significant were observed in between groups (p<0.05)

Table 3: Comparison of heart rate at postoperative monitoring of the study respondents (n=80)

Heart rate	Group-D Mean±SD	Group-F Mean±SD	p value
0 hr. immediate postoperative	78.32±3.91	81.62±3.02	<0.001^S
1st hour after infusion	70.64±3.82	75.14±7.12	<0.001^S
3rd hour after infusion	68.52±6.72	75.84±5.72	<0.001^S
6th hour after infusion	69.54±5.42	72.82±6.74	<0.001^S
9th hour after infusion	68.46±4.33	72.21±5.91	<0.001^S
12th hour after infusion	69.82±4.19	73.30±4.74	<0.001^S
18th hour after infusion	70.56±3.94	73.82±4.11	<0.001^S
24th hour after infusion	69.84±4.21	73.32±4.76	<0.001^S
30th hour after infusion	68.15±3.75	73.41±3.34	<0.001^S
36th hour after infusion	67.38±3.24	72.57±3.40	<0.001^S
48th hour after infusion	68.74±3.10	72.20±3.27	<0.001^S

All values were presented as mean±SD or in frequencies. Data were analysed using unpaired student t-test. Statistically significance was set at p-value <0.05. (S=significance, NS=not significant)

The mean heart rate in postoperative period, were significantly higher in group F in compare with Group D (p<0.05).

Table 4: Comparison of mean arterial blood pressure at postoperative monitoring of the study respondents (n=80)

Mean arterial blood pressure	Group-D (n=40) Mean±SD	Group-F (n=40) Mean±SD	p value
0 hr. immediate postoperative	92.33±7.60	94.84±8.13	0.001^S
1th hour after infusion	91.54±6.90	94.67±7.84	0.001^S
3rd hour after infusion	90.78±5.39	93.92±6.55	0.001^S
6th hour after infusion	90.72±5.35	93.86±6.51	0.001^S
9th hour after infusion	89.62±4.70	93.39±4.36	0.001^S
12th hour after infusion	88.86±3.95	92.74±4.12	0.001^S
18th hour after infusion	88.24±3.40	91.76±4.10	0.001^S
24th hour after infusion	89.30±4.57	91.20±4.07	0.001^S
30th hour after infusion	89.72±4.68	92.46±4.50	0.001^S
36th hour after infusion	88.88±3.95	92.76±4.12	0.001^S
48th hour after infusion	88.28±3.40	91.80±4.10	0.001^S

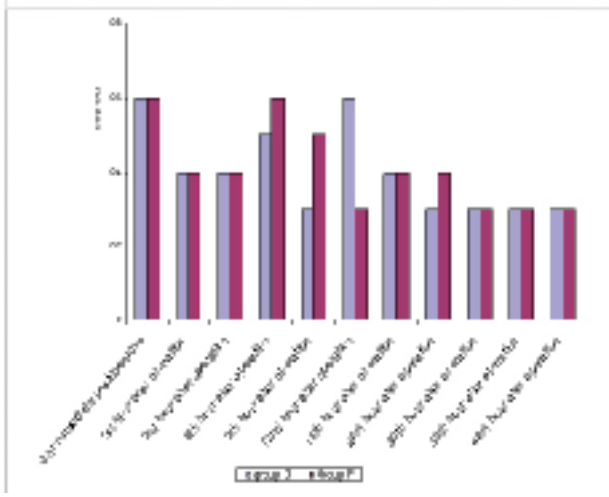


Figure-3: Line diagram showing postoperative VAS score in two groups

The mean VAS at postoperative period compared between two groups. No statistical significance were observed in between groups ($p > 0.05$).

Table 5: Comparison of postoperative complications of the study respondents (n=80)

Complications	Group-D: Case (n=40)	Group-F: Control (n=40)	p value
Nausea and vomiting	04	12	$<0.001^{S}$
Pruritis	00	04	$<0.001^{S}$
Respiratory depression	00	04	$<0.001^{S}$
Urinary retention	00	05	$<0.001^{S}$
Shivering	02	04	0.57^{ns}
Headache	04	03	0.25^{ns}

All values were presented as mean±SD or in frequencies. Data were analysed using unpaired student t-test. Statistical significance was set at p-value <0.05. (S=significance, NS=not significant)

Discussion

Epidural analgesia is considered as the gold standard analgesic technique for major abdominal surgeries. This strategy has the potential to provide complete analgesia and it is particularly effective at optimizing functional pain relief, thus improving patient satisfaction and postoperative outcome.

The use of well-documented physiological advantages of epidural analgesia in such a postoperative care program leads to decrease of morbidity across major abdominal procedures and significantly improves the quality of postoperative recovery.[13,14]

Findings of many clinical trials are relevant in this respect. Thus, patients with major abdominal procedures managed in a multimodal care program including epidural analgesia have demonstrated earlier discharge from intensive -care unit, earlier return of normal bowel function, reduced catabolism and less fatigue than those undergoing equivalent surgery but not participating in such a postoperative care program.[15,13,16]

In our study postoperative analgesia was prolonged significantly in the dexmedetomidine group and consequently the low dose consumption of local anaesthetic was used in dexmedetomidine group, and the same result was shown by other studies.[17-20]

The present study also showed that adding dexmedetomidine as an adjuvant to postoperative epidural bupivacaine (0.125%) decreased the heart rate and the mean arterial blood pressure compared with fentanyl.[1]

These findings correlate with the result of other studies and the decrease in heart rate and mean arterial blood pressure can be explained by the central action of dexmedetomidine in decreasing the sympathetic outflow and catecholamines release.[21,22] Eskander *et al.*[23] found that the heart rate decreased significantly with dexmedetomidine, but the mean arterial blood pressure decreased significantly in the control group compared to dexmedetomidine.

The incidence of sedation before opioid administration was higher in dexmedetomidine compared to fentanyl group, but after opioid administration it was higher in the fentanyl group compared to dexmedetomidine group, and this may be related the sedative effects of opioids required in the fentanyl group more than dexmedetomidine group. Eskander *et al.*[23] showed the same result in spite of the required nalbuphine was higher in the control group and the same result was found by Kurr *et al.*[17] and Gupta *et al.*[25]

The side effects such as nausea, and vomiting, pruritis, urinary retention, and respiratory depression were significantly lower in dexmedetomidine group compared to fentanyl group and a similar result was shown by Gupta *et al.*[23] Bajwa *et al.*[24] found that nausea and vomiting was associated with epidural fentanyl more than dexmedetomidine and no difference in the incidence of pruritis, respiratory depression or urinary retention between the two groups.

Conclusion

Dexmedetomidine is an ideal adjuvant to epidural bupivacaine for postoperative analgesia compared to fentanyl in patients undergoing hepatobiliary pancreatic surgery. Dexmedetomidine provides a better postoperative analgesia and reduces the postoperative opioids related complications compared to fentanyl.

Conflict of interest: None.

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